Consortium Case Study Measuring the Influence of Master Agreements on Execution of Clinical Trial Project Agreements

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Abstract

We measured contract negotiation events to full execution (FE) in a prospective observational study of clinical trial agreements (CTAs) at 17 participating consortium sites. We hypothesized that the use of master agreements (MAs) would significantly reduce the time to FE for project-specific CTAs. A secondary test was planned on a possible difference between "simple" and "complex" agreements, and between different types of sites. Unfortunately, the consortium was dissolved with only one project involving two sites that had signed the MA also signing the Project CTA. This paper reports on the available data. The, admittedly limited, data suggests that MAs may not reduce time to FE of CTAs in particular cases.

Introduction

The Clinical and Translational Science Awards (CTSA) Program (https://ncats.nih.gov/ctsa) reported that an average contract terms negotiation time of 55 days could be reduced to 22 days if a 'master agreement' was used.[1] This inspired the Accelerated Research Agreements Initiative (https://www.ara4us.org) to develop standard agreements and sign members who could agree to accept standard agreement terms and conditions. Other organizations, like the Model Agreements & Guidelines International (MAGI) (https://www.magiworld.org/Overview) group, have long been active in hosting clinical research events for any parties interested in standardizing best practices for clinical operations, business and regulatory compliance. Indeed, the Federal Demonstration project (https://thefdp.org/default/) created in 1986 has the federally mandated goal of reducing the administrative burdens associated with research grants and contracts. One of its first products for reducing contracting bottlenecks was a standard template for subcontracting work on research grants. In addition, studies have investigated process improvement impact on FE.[2] Reducing the time to FE, or at least accurately estimating it, is a significant concern in research administration. Efforts to measure time to FE will continue, and more data will help us understand how to manage contracting bottlenecks in research administration.

Study Background

Over 50 individual investigators and affiliated consortium individuals working at 42 different member institutions joined a cancer research consortium hosted by our small non-profit company. The MA terms and conditions were drafted from experience with generally accepted academic principles, and using examples from the CTSA Program and MAGI. Liability in the MA was minimal with no monetary obligation, collegial participation, and standard confidentiality language. This at least covered the effort needed to negotiate mutual confidentiality agreement (CDAs) for protocol review on possible consortium projects. MA negotiation events centered on confidentiality, intellectual property, publication and indemnification. Time to FE was adjusted as revisions to MAs signed by early adopters were later amended with more expansive terms and conditions that were negotiated and accepted by members who signed later (e.g., 30-day publication delays rather than a 90-day review). We considered this experience to characterize a "simple" agreement because of the low liability and common terms and conditions. 17 sites signed a MA, although other sites and sponsors were admitted to the consortium under the bylaws when approved by a majority of the 17 core members.

Methods

Agreements were sent April 2018 with 2018-04-15 set as the "baseline" for tracking interactions with the sites. Their names were changed for this study to classify their institutional type and geographical location:

Cancer Center AZ
Cancer Center OH
Clinic 1 NJ
Clinic 2 AZ
Cooperative LA
Cooperative TX
Cooperative SW
Hospital Korea
Hospital PA
Hospital Spain
Hospital WA
University CO
University IL
University MD
University OH
University PA
University WI

The time to FE for managing these agreements was recorded by event on each date of interaction. Categories of interactions were recorded, with status checks, (223), exchange of redlined agreements (61), and questions (30), primarily describing the types of events. The median time to FE for all sites was 94 days, ranging from Clinic 1 who signed in 3 days to our most reluctant member who took 219 days.

Table 1

Record of interaction events to full execution in negotiation of a consortium Master Agreement

baseline	questions	status checks	redlines	FE
41	30	223	61	17

"baseline" is day 1 for the 41 site invitations to sign an MA, "questions" reflect events where a question about the consortium was answered, "status checks" are events in follow-up, "redlines" are events where negotiated terms and conditions were exchanged, and "FE" is for the fully executed 17 MA events.

Results

The plot below displays all interactions for the 17 sites that executed an MA.

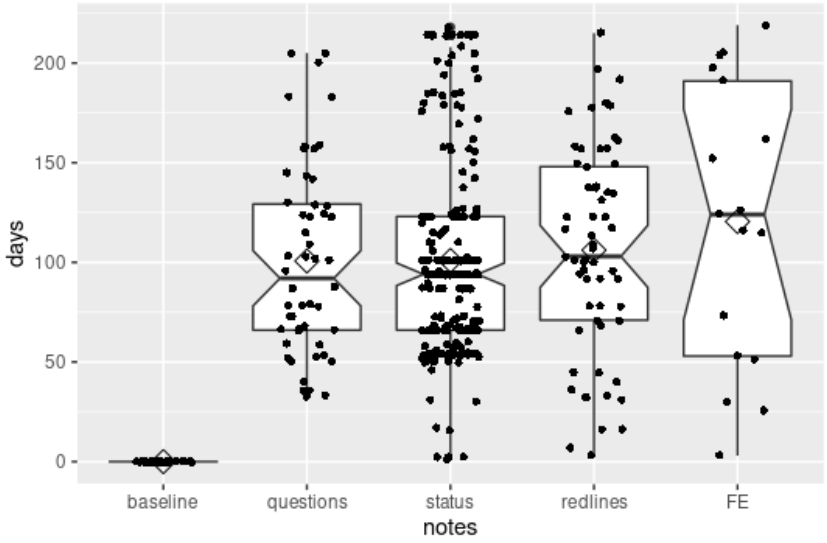


Fig. Time to FE for consortium Member Agreements

There are noticeable differences between the 3 days it took to sign an agreement with Clinic 1 NJ to the 200+ days it took for some large cancer centers and universities. Although the team generally knew which sites were amenable to agreement, the quantitative measures were useful for presentation. A larger sample size would be needed to determine differences for the category types (e.g. hospital versus university).

The first consortium project was also considered to be a simple agreement. It was a minimally invasive specimen collection protocol for saliva, serum and blood, with low liability for subject injury and pooled genomic data for anonymity. The number of days to FE on the Project CTA were similar to the number of days to FE on the MA for the two sites who signed both. Time to FE for all sites had a median of 131 days ranging from 73 to 268 days.

Table 2

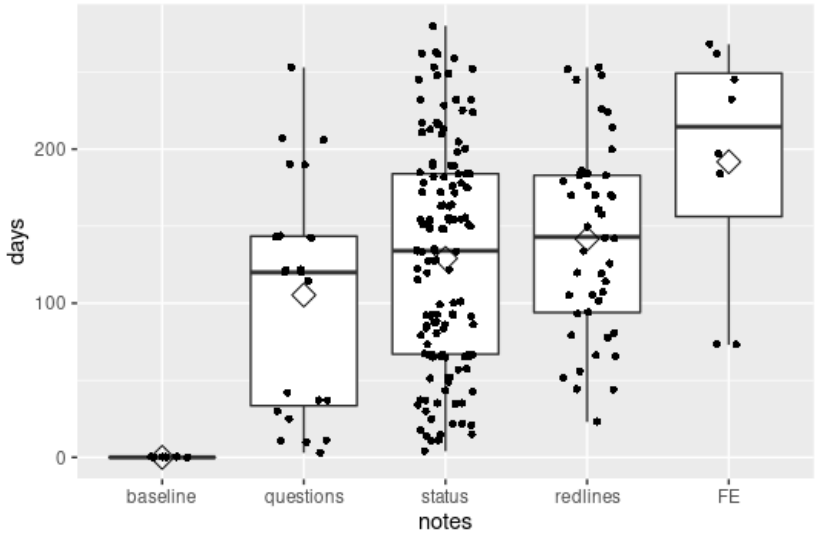
Total number of days to FE by participating site, including days to FE for two sites that also signed the consortium MA.

Participating Site	days to FE for the MA	days to FE for the Project CTA
Hospital AZ	71 days	73 days
Cancer Center OH	232 days	268 days
Hospital MN		232 days
University MO		184 days
Cooperative SW		197 days
Sponsor		245 days

Type of events for the specimen collection project had a distribution similar to the MA contract negotiations. Time to FE was also tracked for the company sponsor. Note that site agreements were possible before the actual sponsor agreement was executed.

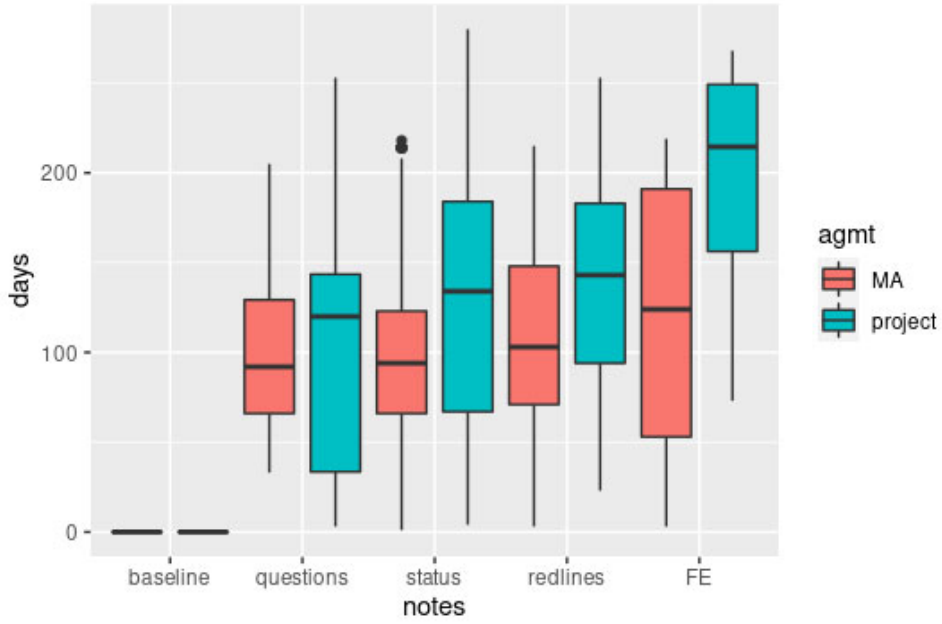
Total number of interaction events:

Hospital AZ	19
Hospital MN	39
Cancer Center OH	40
University MO	26
Cooperative SW	44
Sponsor	27



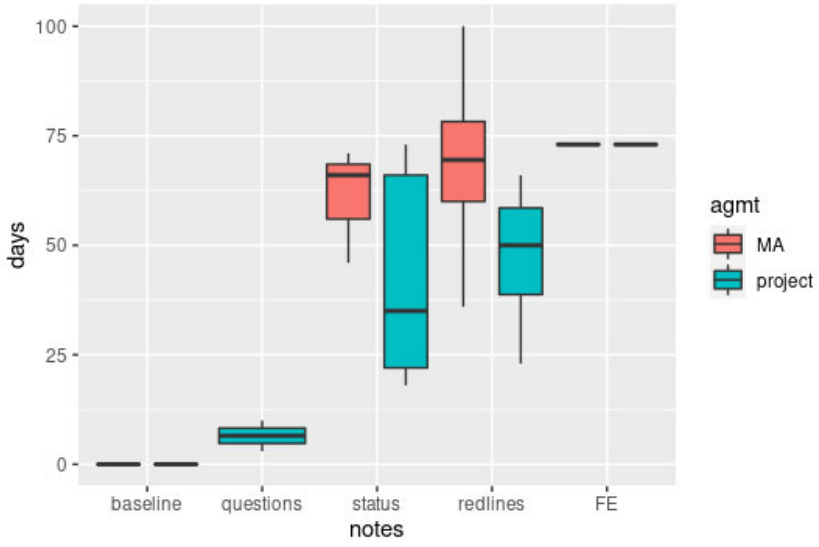
Time to FE for the consortium Project .

Although we don't have enough data to reject the hypothesis that MAs can reduce the time to FE project agreements, there was no significant difference for the three Members who later participated in the first consortium Project. In general, time to FE for the MA correlates with the Project Agreement (PA). Member-sites who considered participating in the specimen collection project, but later withdrew are not included because they did not reach the endpoint (and I don't know how to do the stats for that!)



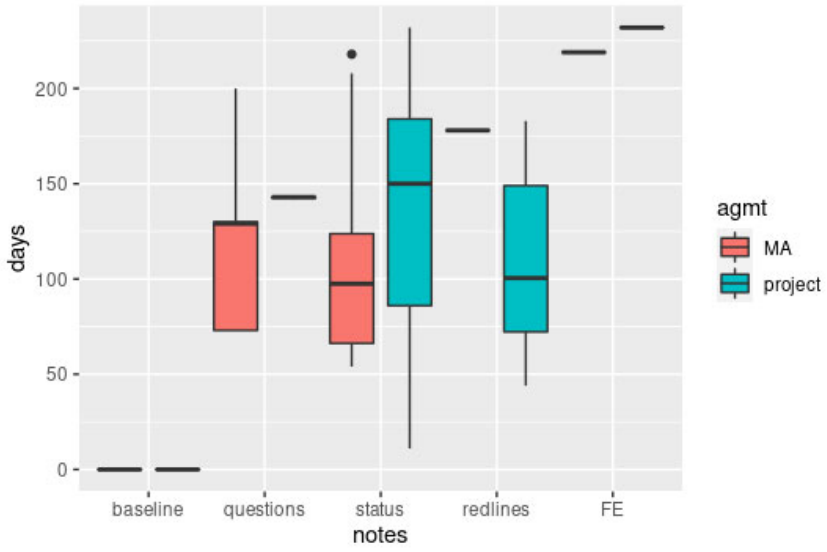
Time to FE for the MA compared to the consortium project

Differences in the type of interaction also varied for members who signed a project agreement. This suggests that particular project issues might supersede general agreement principles, but also provides evidence that a sites response to the project agreement was influenced by the MA. The health center in Arizona, for example, had more redlines on the MA than the PA, and signed both agreements in 70+ days.



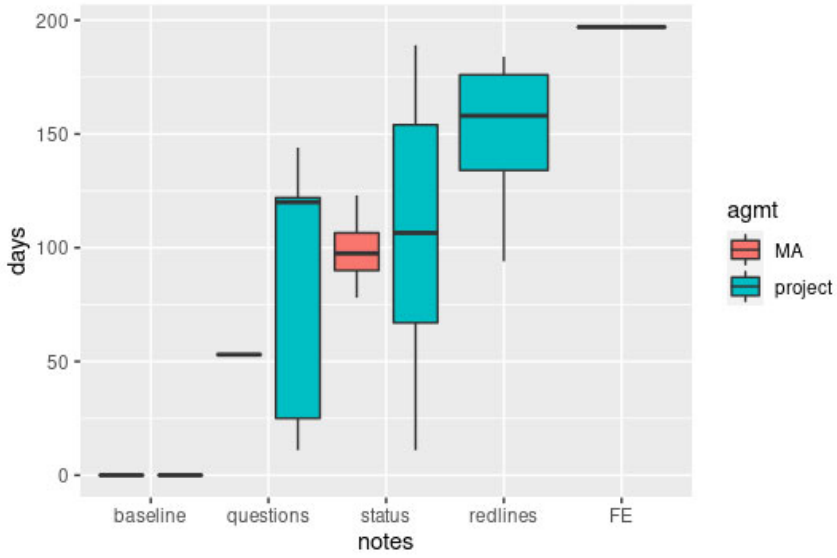
Time to FE for the MA compared to the consortium project in AZ

A health center in Ohio, in contrast had many questions about the MA and no questions about the PA. They did, however, have many more redlines on the PA than on the MA, but their time to FE was not significantly reduced.



Time to FE for the MA compared to the consortium project in AZ

Consortium members included sites that declined to sign an MA. Several of these participated in the Project, but the impact of discussions around the MA had little to no effect on the project agreement time to FE. They typically had questions about the MA, and ultimately declined with few or no redline exchanges.



Time to FE for a project site in Missouri that declined to sign an MA

Data for time to FE on an IST project was also collected. This entailed a complex agreement with proprietary product from two drug companies, tumor collection in surgery, and the expectation of multiple adverse events. This project only opened at one site, and later closed in the first round of dose escalation for the phase I trial. Data for the type of events and time to FE are not sufficient to test the idea about a difference between simple and complex clinical trial agreements. And, the sponsor-investigator's institution only signs MAs with large drug companies.

Conclusion

Healthcare provider, company sponsors, and research administrators in the clinical trial business want to know how long it takes to sign agreements. Such measures are important for planning studies concurrent with scientific review, human subject use (IRB), and budget negotiation. This paper presents data on types of events in contracts management to time of FE for members of a cancer research consortium. Time and events to the MA execution process were observed, but there were not enough projects to test the hypothesis that MAs would significantly reduce time to FE for PAs. This data, however, does not support the hypothesis that a general master agreement for a consortium of sites will reduce the time needed to execute particular project agreements with particular sites. In this study, there was a significant difference in time to FE between sites, and a possible difference between types of institution, but, again, not enough data to identify general trends. Our effort to track interaction events in a grants and contracts office demonstrates that making these measures is possible, and provides evidence for the value of ongoing studies that track events for time to FE using model agreement terms and conditions. More data from similar studies could provide greater insight into how to handle the bottleneck of agreement execution in research management.

References

[1] Observational study of contracts processing at 29 CTSA sites. Clin Transl Sci. 2013 Aug;6(4):279-85.Kiriakis,J, Gaich N, Johnston SC,Kitterman D, Rosenblum D, Salberg L, Rifkind A.

[2] Saha, D. C., Ahmed, A., Hanumandla, S. (2011) Expectation-based efficiency and quality improvements in research administration: Multi-institutional case studies. Research Management Review. 18(2):1-22

Doug is a veteran research administrator with a BS in Geology from Western Kentucky University, and a Master's in History from the University of Utah. He has worked at the University of Washington since 1990, initially providing support for the Boeing Back Pain Study before moving to central services in the Office of Sponsored Programs. He also worked for a private non-profit research company, Cancer Research And Biostatistics, supporting the SWOG cooperative group funded by the NIH NCI NCTN and NCORP, where he published on liability issues affecting sponsor-investigator clinical trials. Doug returned to the University in 2016, working for the Cancer Vaccine Institute as a Grants and Contracts Manager.